

### **REMARKS**

Applicants request entry of this amendment and reconsideration of the rejection of the claims.

Applicants have amended claims 1 and 24. Applicants submit the amendments are supported throughout the specification and do not represent new matter.

Applicants have cancelled claim 25 without prejudice or disclaimer. Applicants reserve the right to pursue the subject matter of these claims in one or more continuation applications.

### **35 U.S.C. § 103**

The examiner rejected claims 1-6 under 35 U.S.C. § 103 in view of Qiagen in view of U. S. Patent No. 5, 480, 972 ('972) and U. S. Patent No.6,177,278 ('278) and Webster's Dictionary. Applicants respectfully traverse.

To make a *prima facie* case of obviousness, the teachings of the prior art should have suggested the claimed subject matter to the person of ordinary skill in the art, and all the claim limitations must be taught or suggested in the references cited by the Examiner. *In re Kotzab*, 217 F.3d 1365, 1370 (Fed. Cir. 2000). As articulated by the Supreme Court in a recent case, a combination is obvious if it is no more than the predictable use of known elements according to their established functions; and there was a reason to combine the known elements. *KSR Int'l Co. v. Teleflex, Inc.*, 550 U.S. \_\_\_ (2007). To make a *prima facie* case of obviousness, "it remains necessary to identify the reason why a person of ordinary skill in the art would have combined the prior art elements in the manner claimed." *Id.* A dependent claim is not obvious if the claim from which it depends is not obvious. *In re Fine*, 837 F.2d 1071 (Fed. Cir. 1988). The initial burden to make a *prima facie* case of obviousness is on the Examiner. *In re Bell*, 991 F.2d 781, 783 (Fed. Cir. 1993). Applicants submit that the Examiner does not make a *prima facie* case of obviousness, because all the limitations of the present claims are not taught by the combination of references cited in the Office Action and there would be no reason to combine the references.

Applicants claim 1 is now directed to a method of preparing a sample substantially free of genomic DNA, comprising: forming a tissue or cell lysate from a biological sample, wherein said lysate contains genomic DNA; contacting a pre-filtration column with said lysate, wherein

said pre-filtration column comprises a filter material, wherein said filter material has at least one layer of glass or borosilicate fiber, whereby genomic DNA is bound to said filter material; collecting effluent from said column, wherein said effluent is substantially free of said genomic DNA; contacting a silicon carbide whisker column with said effluent of (c), whereby nucleic acids comprising RNA are bound to said silicon carbide; and eluting said RNA from said silicon carbide whisker column.

Applicants submit that the Qiagen reference does not disclose at least the steps of collecting the effluent from the prefiltration column and contacting the effluent with a silicon carbide whisker column, whereby nucleic acids are bound to the silicon carbide column. The Qiagen column binds both DNA and RNA and allows elution of DNA or RNA at different salt concentrations. Since the method described in the reference is a method for isolating RNA and DNA from each other there would be no need to prefilter the lysate or contact the effluent to a silicon carbide whisker column. In addition, the material used to bind DNA in the Qiagen et al reference is an anionic resin and there is no teaching or suggestion of the use of a glass or borosilicate filter to bind genomic DNA. In fact, such a filter would not be necessary since the anionic resin binds the DNA, as well as RNA. The effluent flowing through the column without any elution buffer should not contain either DNA or RNA as both bind the column.

The method of Qiagen employs a different separation strategy than the method of Applicants, and thus these methods are not interchangeable with one another. In Qiagen et al., a single column is used to bind both RNA and DNA and then either can be selectively eluted depending on the salt conditions. In contrast, Applicants method involves two different columns, one of which binds the genomic DNA and does not bind RNA.

The deficiencies in the Qiagen et al. reference are not remedied by reference to the '972 or '278 patent. The '972 patent describes isolation of RNA using an oligo dT column. There is no teaching or suggestion of a prefiltration column comprising a glass or borosilicate filter that binds genomic DNA. Moreover, the two columns discussed by the examiner are the same type of column – both are oligo dT columns. There is no discussion of collecting the effluent from the prefiltration column and contacting the effluent with a silicon carbide whisker column, whereby nucleic acids are bound to the silicon carbide column. In fact, the effluent of this column (in the

absence of elution buffer) would contain DNA and not RNA. Thus, even in combination with Qiagen the references do not teach all of the elements of the claims.

The '278 patent is directed to isolation of DNA and RNA using a silicon carbide column. There is no discussion in this reference of using a prefiltration column comprising a glass or borosilicate filter that binds genomic DNA, as such a filter would not be necessary as DNA binds to the silicon carbide column. In addition, this patent indicates that both DNA and RNA are bound to the column and does not provide any information about how DNA can be separated from RNA using the silicon carbide column. Moreover, this column does not include silicon carbide whiskers but rather silicon carbide grit which has significantly less surface area than that of silicon carbide whiskers. See the specification at page 8, lines 10-12. Thus, even when combined with the other cited references, all of the elements of Applicants claims are not disclosed.

In addition, applicants submit one of ordinary skill in the art would not have a reason to combine these references as at least, the Qiagen et al reference and the '972 patent are directed to methods using different separation strategies using a different types of resin. In the case of Qiagen et al, the reference is directed to using a single resin to bind both DNA and RNA. The resin which binds DNA and RNA is an anionic resin. There is no mention of preparing a sample substantially free of genomic DNA. Secondly, the '972 reference is directed to using an oligo dT column to bind mRNA. These types of resin are different from either the glass or borosilicate filter or the silicon carbide whisker column. Finally, the '278 reference describes isolation of RNA and DNA and does not teach or suggest preparing a sample free of genomic DNA using a two different columns with different binding capability. Applicants submit that one of skill in the art would not combine these methods because the type of resins used are not interchangeable and do not serve the same purpose, and the 278' patent indicates that the silicon carbide column binds both DNA and RNA.

Based on the foregoing, Applicants request withdrawal of the 35 U.S. C. 103 rejection.

The examiner rejected claim 7 under 35 U.S.C. § 103 in view of Qiagen in view of U. S. Patent No. 5, 480, 972 ('972) and U. S. Patent No.6,177,278 ('278), Webster's Dictionary and further in view of U. S. Patent No. 3,414,394 ('394). Applicants respectfully traverse.

As discussed above, the cited references do not teach or suggest all of the elements of the claims and there would be no reason to combine these references. The arguments concerning Qiagen, '972 patent, and '278 patent are incorporated herein.

The '394 patent does not remedy the deficiencies of any of the cited references. This reference is directed to forming a glass filter. There is no discussion in this reference of a prefiltration column comprising a glass or borosilicate fiber, or contacting effluent from the prefiltration column with a silicon carbide whisker column. The only sample type mentioned is water. Thus, even when combined with the other cited references, all of the elements of the claims are not disclosed. Applicants request withdrawal of the rejection.

The examiner rejected claims 8 under 35 U.S.C. § 103 in view of Qiagen in view of U. S. Patent No. 5, 480, 972 ('972) and U. S. Patent No. 6,177,278 ('278), Webster's Dictionary and further in view of U. S. Patent No. 6,383,393('393). Applicants respectfully traverse.

As discussed above, the cited references do not teach or suggest all of the elements of the claims and there would be no reason to combine these references. The arguments concerning Qiagen et al., '972 patent, and the '278 patent are incorporated herein.

The '393 patent does not remedy the deficiencies of any of the cited references. This reference is directed to isolating nucleic acids from other cell components, in particular, isolation of DNA. There is no discussion in this reference of a method for preparing a sample free of genomic DNA using a prefiltration column comprising a glass or borosilicate fiber, or contacting effluent from the prefiltration column with a silicon carbide whisker column. Thus, even when combined with the other cited references, all of the elements of the claims are not disclosed. Applicants request withdrawal of the rejection.

The examiner rejected claim 9 under 35 U.S.C. § 103 in view of Qiagen in view of U. S. Patent No. 5, 480, 972 ('972) and U. S. Patent No. 6,177,278 ('278), Webster's Dictionary and further in view of Aldrich Chemical Company Catalog. Applicants respectfully traverse.

As discussed above, the cited references do not teach or suggest all of the elements of the claims and there would be no reason to combine these references. The arguments concerning Qiagen et al., '972 patent, and the '278 patent are incorporated herein.

The Aldrich Chemical Catalog does not remedy the deficiencies of any of the cited references. This reference is directed to describing glass filters. There is no discussion in this reference of a prefiltration column comprising a glass or borosilicate fiber, wherein the genomic DNA is bound to said filter material or contacting effluent from the prefiltration column with a silicon carbide whisker column. Thus, even when combined with the other cited references, all of the elements of the claims are not disclosed. Applicants request withdrawal of the rejection.

The examiner rejected claims 24-36 under 35 U.S.C. § 103 in view of Qiagen in view of U. S. Patent No. 5, 480, 972 ('972) and U. S. Patent No.6,177,278 ('278), Webster's Dictionary and further in view of U.S.Patent No.5,006,472 ('472). Applicants respectfully traverse.

As discussed above, the cited references do not teach or suggest all of the elements of the claims and there would be no reason to combine these references. The arguments concerning Qiagen et al., '972 patent, and the '278 patent are incorporated herein.

The '472 patent does not remedy the deficiencies of any of the cited references. This reference is directed to contacting a sample with a DNAase. There is no discussion in this reference of a prefiltration column comprising a glass or borosilicate fiber, wherein the genomic DNA is bound to said filter material or contacting effluent from the prefiltration column with a silicon carbide whisker column. The only separation methods identified include precipitation, ion exchange, and size exclusion. Thus, even when combined with the other cited references, all of the elements of the claims are not disclosed. Applicants request withdrawal of the rejection.

The examiner rejected claim 37 under 35 U.S.C. § 103 in view of Qiagen in view of U. S. Patent No. 5, 480, 972 ('972) and U. S. Patent No.6,177,278 ('278), Webster's Dictionary and further in view of U.S.Patent No.5,006,472 ('472) and U.S.Patent No. 4,996,144('144). Applicants respectfully traverse.

As discussed above, the cited references do not teach or suggest all of the elements of the claims and there would be no reason to combine these references. The arguments concerning Qiagen et al., '972 patent, and the '278 patent are incorporated herein.

The '144 patent does not remedy the deficiencies of any of the cited references. This reference is directed to detecting RNA or DNA in cells using hybridization. Samples are treated with RNAase or DNAase to remove either RNA or DNA respectively, before hybridization.

There is no discussion in this reference of a prefiltration column comprising a glass or borosilicate fiber, wherein the genomic DNA is bound to said filter material or contacting effluent from the prefiltration column with a silicon carbide whisker column. Thus, even when combined with the other cited references, all of the elements of the claims are not disclosed. Applicants request withdrawal of the rejection.

### SUMMARY

In view of the above amendments and remarks, Applicant respectfully requests a Notice of Allowance. If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

Respectfully submitted,

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